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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/633,034	08/04/2000	Kwong Y. Tsang	A33081	2330

21003 7590 05/07/2004

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EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/633,034	TSANG ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Reissue Applications

1. Claims 1, 30, 33, 34, 36, 37, 38, have been amended.

2. Claims 1-50 are pending and under examination.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

4. The following Office Action contains NEW GROUNDS of rejections.

5. Applicant is reminded of the continuing obligation under 37 CFR 1.178(b), to timely apprise the Office of any prior or concurrent proceeding in which Patent No. 5,688,657 is or was involved. These proceedings would include interferences, reissues, reexaminations, and litigation.

6. Applicant is further reminded of the continuing obligation under 37 CFR 1.56, to timely apprise the Office of any information which is material to patentability of the claims under consideration in this reissue application.

7. These obligations rest with each individual associated with the filing and prosecution of this application for reissue. See also MPEP §§ 1404, 1442.01 and 1442.04.

8. The original patent, or a statement as to loss or inaccessibility of the original patent, must be received before this reissue application can be allowed. See 37 CFR 1.178.

Amendments

9. The amendment filed 3/15/04 proposes amendments to the claims that do not comply with 37 CFR 1.173(b)(2), which sets forth the manner of making amendments in reissue applications.

Any changes to the text of a claim (original or new) must be presented as an entire numbered claim. All subject matter being **added** to an original patent claim **must be underlined**. All subject matter being **deleted** from an original patent claim **must be placed between brackets**. 37 CFR 1.173(b((2) and (d). Brackets and underlining are to be used to reflect only those changes in the text from the original patented text and not from any previous amendment in the reissue application see 37 CFR 1.173(g).

Claims 30 and 34 has strikethrough and underlines that delete and add the same text. It appears that claim 1 has not been amended relative to the issued patent. In addition, claims 30, 33 have been amended without brackets or underlining. Claim 30 does not have the second container as recited in the patented claim and this appears to be a typographical error and the claim will be examined as reciting "a second container adapted to contain a second antibody to said antigen or active component thereof". In addition, claims 33 and 37 recite a typographical error in the term "conation" as it should be "container" as indicated in the patented claims 33 and 37. The amendment to claim 30 was without brackets to remove the second container phrase. A supplemental paper correctly amending the reissue application is required. Applicant is reminded that in a re-issue application the amendments need only be for the claims currently amended.

The entire claim set is not needed in a re-issue application. In addition, Applicant is requested to proof read any amendments to help insure that no changes are made to the patent improperly.

Specification

10. The disclosure is objected to because of the following informalities:

a. The specification has been amended to delete the date of deposits for PCA 31.1 and PCA 33.28 and chimeric 31.1. Amendment of the specification to recite the date of deposit is required (see 112 first rejection below).

The amendment to the specification in column 3, line 58 through column 4, line 2 is improper because it is not amended relative to the patent. The hyphen is missing in the "HB 12315" in the amendment. This amendment does not comply with 37 CFR 1.73(b).

Appropriate correction is required.

Claim objections

11. Claims 30, 33, 37 are objected to for the following:

a. Claim 30 does not have the second container as recited in claim 34 and this appears to be a typographical error and the claim will be examined as reciting "a second container adapted to contain a second antibody to said antigen or active component thereof".

b. Claims 33 and 37 recite a typographical error in the term "conation" as it should be "container".

c. Claim 2 of the patent recites "3328" in the last line and should be "33.28".

Appropriate correction is required.

Rejections Withdrawn

12. The rejection of claims 33, 36, 37 under 35 U.S.C. 112, second paragraph, in parts b and c in the previous office action as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

13. The rejection of 44 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

14. The rejection of claims 1, 8-9 under 35 U.S.C. 102(b) as being anticipated by Herlyn et al (PNAS 76:1138, 3/79) is withdrawn in view of the new grounds of rejection.

15. The rejection of claims 1, 8 under 35 U.S.C. 102(b) as being anticipated by Hollinshead et al (Cancer 56:480-489, 1985) is withdrawn in view of the new grounds of rejection.

16. The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Price et al (IRCS Journal of Medical Science 13:366-367, 1985) is withdrawn in view of the new grounds of rejection.

17. The rejection of claims 1, 7-15, 30-33, 36-37, 42, 44, 45, 48 under 35 U.S.C. 103(a) as being unpatentable over Hollinshead et al (Cancer 56:480-89, 1985) as applied to claims 1 and 8 above, and further in view of Neuberger et al (WO 86/01533, published 3/86) is withdrawn in view of the new grounds of rejection.

18. The rejection of claims 1, 7-15, 30-33, 36-37, 42, 45, 48 under 35 U.S.C. 103(a) as being unpatentable over Herlyn et al (PNAS 76:1138, 1979) or Price et al (IRCS Journal of Medical Science 13:366, 1985) and further in view of Neuberger et al (WO 86/01533, published 3/86) is withdrawn in view of the new grounds of rejection.

Response to Arguments

19. The rejection of claims 1-50 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention as indicated in part (a) of the previous office action is maintained.

The response filed 3/15/04 has been carefully considered but is deemed not to be persuasive. The response states that the claims have been amended to recite "said antigen is free of HLA-antigen and substantially free of non-immunogenic glycoproteins" (see page 6 of response). In response to this argument, claims 1, 30, 34, 38 have been amended but they have been amended to recite the exact language that is stricken though in the amendment, therefore not altering the language of the claims. The phrase "said antigen is purified to the extent that the membrane fractions are free of HL-A

antigen and are substantially free from non-immunogenic glycoprotein fractions" is still indefinite as indicated in the previous Office Action as it has not been amended as stated in the response filed 3/15/04. As such the rejection is maintained.

20. The rejection of claims 2-6, 17-29, 34-35, 38-41, 43, 47, 49-50 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is maintained.

NOTE: The papers filed 8/29/03 to verify deposit of the biological materials which contains copies of the forms sent to the ATCC had the credit card number and expiration date of a visa card. This set of papers was scanned into the image file which is now the working record for this application. Because this information could have been available to employees at the USPTO as well as members of the public the papers were removed from viewing in this application. As such it is requested that a complete copy of all papers filed with the papers of 8/29/03 be resubmitted without the credit card information (blacked out for example). Then these papers will complete the record and be able to be viewed.

The response filed 3/15/04 has been carefully considered but is deemed not to be persuasive. The specification has been amended to remove the deposit date and as such all requirements have not been made and all claims reciting 33.28, 31.1, Chi#1 are

included in the rejection. The response states that hybridoma cell lines 33.28, Chi#1, and 31.1 have been deposited at the ATCC and the statement of Dr. Arlen states that the biological material described in the specification is the same as that deposited (see page 7 of response). In response to this argument, the statement of Dr. Arlen is not in the form of a declaration and additionally the statement is for "31.1" and "33.28" and the specification describes the hybridomas as "PCA 31.1" and "PCA 33.28" (see column 3, line 58 through column 4, line 2 (amended in this response). Thus, it is not clear if the hybridomas deposited are the same as those recited in the specification or in the claims. In addition, it is not clear why the "PCA 31.1" was given a new ATCC number, while the "PCA 33.28" was not when both were redeposited due to the mistake associated with the deposit at the ATCC as stated in the declaration filed with the reissue and this is the reason for the filing of the reissue application. In addition, claims that recite the 31.1 antibody have not been amended to recite the new ATCC number of "PTA-2497" and as such it is unclear if this hybridoma has been deposited or if it is different from the one designated "ATCC HB-12314".

If new deposits are made then all assurances of public availability must be met.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

21. The rejection of claims 1, 7-16, 30-33, 42, 45-46, 48 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in

such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 3/15/04 has been carefully considered but is deemed not to be persuasive. The response states the claims are directed to monoclonal antibodies that bind an antigen with four different identifying characteristics and the specification clearly demonstrated the production of monoclonal antibodies that bind the antigen (see page 7-8 of response). In response to this argument, the rejection was not a 112 first enablement rejection of how to make an antibody. The rejection is for written description. The specification only teaches a 61.1 kD protein and a 72 kD protein with the claimed characteristics. No other antigen are disclosed in the specification. The claims are broadly drawn to any molecular weight protein with the claimed characteristics, however, no other antigens are disclosed as having the claimed characteristics. The claims do not contain any structural characteristics of the antigen, just functional characteristics. As such it would reasonable to conclude to one of skill in the art that the inventor(s) at the time of the application was filed did not have in their position the claimed invention. Thus the rejection is maintained.

The following are NEW GROUNDS of rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

22. Claims 1, 8-9, 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Herlyn et al (PNAS 76:1138, 3/79).

The claims recite an antibody specific for an antigen characterized by a purification and wherein the antigen is not detected on human carcinoma cells other than colon and is not detected on normal tissue and the antigen is immunogenic in humans and induces an immune response and is radiolabeled. Claim 16 is included in the rejection and is interpreted to mean an antibody that binds to the Fc region of the antibody in claim 1 which is interpreted to be a secondary antibody (see page 1439).

Herlyn et al teach antibodies to antigens from colon carcinoma cells and the antibody does not bind to normal cells and the antibody is radiolabled (see abstract and entire document). In addition, it would be inherent that the antigen would induce an immune response in humans because the antigen is not found in normal tissue.

Herlyn is silent as to the characterization of the antigen but teaches the antigen is from colon carcinoma cells and does not bind to normal cells and because the antigen is not in normal cells the antigen would inherently have the property of inducing an immune response. Therefore, it is the Examiner's position that Herlyn et al have produced hybridomas which secrete antibodies that are directed to the same antigen that the claimed antibodies bind. One of ordinary skill in the art would reasonably conclude that Herlyn's antibody also possesses the same structural and functional properties as those of the antibodies claimed and, therefore, it appears that Herlyn have produced hybridomas that secrete antibodies that are identical to the claimed antibody. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed hybridoma and antibody with the hybridoma and antibody of Herlyn, the burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The response filed 3/15/04 has been carefully considered but is deemed not to be persuasive. The response states that Herlyn does not disclose molecules capable of cell mediated immunity and the antibodies of Herlyn fail to bind to SW480 cells where as Applicants antibodies bind to the SW480 cells (see response at page 8-9). In response to this argument, the claims do not require binding to any specific cells and as such applicants are arguing limitations that are not in the claims. In addition, just

because Herlyn does not disclose a characteristic of cell mediated immunity does not demonstrate that the antibodies do not have this property. As indicated in the rejection it would be inherent that the antigen would induce an immune response in humans because the antigen is not found in normal tissue.

Thus the art reads on the claims.

23. Claims 1, 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Hollinshead et al (Cancer 56:480-489, 1985).

The claims have been described supra.

Hollinshead et al teach monoclonal antibody to a colon carcinoma which induces an immune response (see page 481) and the antigen is not present in normal tissue (see page 487) and the antibody is used in an ELISA (see page 487).

Hollinshead et al's antigen is described as being a colon carcinoma antigen which induces an immune response and is not present in normal tissue.

It is the Examiner's position that Hollinshead et al have produced hybridomas which secrete antibodies that are directed to the same antigen that the claimed antibodies bind. One of ordinary skill in the art would reasonably conclude that Hollinshead's antibody also possesses the same structural and functional properties as those of the antibodies claimed and, therefore, it appears that Hollinshead have produced hybridomas that secrete antibodies that are identical to the claimed antibody and bind the same antigen claimed. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody

of Hollinshead, the burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The response filed 3/15/04 has been carefully considered but is deemed not to be persuasive. The response states that Hollinshead merely discloses the purification of two TAA and Hollinshead only mentions the characterization of antibodies to TAA and such characterization is missing and Hollinshead refers to the publication of such characterization as "in preparation" (see page 9 of response). In response to this argument, Hollinshead teaches the characterization of the antigens which are identical to those claimed. In addition Hollinshead teaches the monoclonal antibodies to such antigens as recited in the claims. With reference to the "in preparation" publication, it is unclear what the publication is to disclose since it is "in preparation". The manuscript could be for an assay or something else. Specifically at page 487, Hollinshead recites "Characterization of monoclonal TAA antibodies for use in monitoring Phase III trials were possible because of this trial" and this is a reference to the "in preparation" manuscript. Thus, it seems that the monoclonal antibodies bind to the TAA's disclosed in the reference.

24. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Price et al (IRCS Journal of Medical Science 13:366-367, 1985).

The claim has been described supra.

Price et al teach an antibody to a colon carcinoma antigen wherein the antigen is in colon carcinoma cells and not in normal colon cells (see Table page 367). Since the antigen is in carcinoma cells and not in normal cells it would be inherent that the antigen induces an immune response in humans.

Price teach the antigen is a colon carcinoma antigen and is not in normal tissue and it would inherently induce an immune response and Price is silent as to the purification characterization of the antigen, however, it is the Examiner's position that Price have produced hybridomas which secrete antibodies that are directed to the same antigen that the claimed antibodies bind. One of ordinary skill in the art would reasonably conclude that Price's antibody also possesses the same structural and functional properties as those of the antibodies claimed and, therefore, it appears that Price have produced hybridomas that secrete antibodies that are identical to the claimed antibody and bind the same antigen. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody of Price, the burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The response filed 3/15/04 has been carefully considered but is deemed not to be persuasive. The response states that Price describes the production of antibodies to

CEA which in contrast Applicant's antibodies are generated against proteins other than CEA as taught in column 21, lines 63-66 of the specification (see page 10 of response). In response to this argument, while the antibody of Price is directed to CEA, the claims recite nothing about the molecular weight of the antigen or the antibody does not bind CEA. Applicant is arguing limitations that are not in the claim.

25. Claims 16-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Hopp et al (US Patent 4,703,004, filed 6/84) as evidenced by the specification.

The claims recite an antibody against the antibodies of claims 1-6. The claims are interpreted to mean a secondary anti-IgG antibody to the antibody of claims 1-6.

Hopp et al teach secondary antibodies that are anti-IgG antibodies (see column 17, lines 20-40). As evidenced by the specification the 33.28, 31.1 and chimeric antibodies are IgG isotype (see column 25).

26. Claims 1, 7-23, 30-33, 36-37, 42, 44, 45, 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hollinshead et al (Cancer 56:480-89, 1985) as applied to claims 1 and 8 above, and further in view of Neuberger et al (WO 86/01533, published 3/86).

Claims 1 and 8 have been described supra. Claims 7-23, 30-33, 36-37, 42, 44, 45, and 48 recite wherein the antibody is radiolabel, secondary antibody, on a solid phase, labeled with a cytotoxic radiolabel, a cytotoxic drug or protein, immunoassay for detection, compositions comprising such, the antibody is a chimeric antibody, wherein

the antigen is 72 kD and a method of diagnosing comprising removing a specimen and contacting the sample with a chimeric antibody and staining the specimen and detecting the complex. kits comprising an antibody and a second detection antibody. Claims 16-22 and 46 are included in the rejection and are interpreted to mean an antibody that binds to the Fc region of antibody in claims 1-6 and 42 which is interpreted to be a secondary antibody.

Hollinshead et al has been described supra. Hollinshead does not teach a chimeric antibody or an antibody labeled with a cytotoxin, radiolabel, a kit comprising an antibody and a second antibody and a substrate for the enzyme, or a method of diagnosing colon cancer with a chimeric antibody. These deficiencies are made up for in the teaching of Neuberger et al.

Neuberger et al teach chimeric antibodies and antibodies that can be labeled with toxins, radiolabels, dyes, cytotoxic agents (see page 7) and the antibody can be immobilized for affinity chromatography (see page 8).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have labeled the antibody and produce a chimeric antibody in view of Hollinshead et al and Neuberger et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have labeled the antibody and produce a chimeric antibody in view of Hollinshead et al and Neuberger et al because Hollingshead et al teach the antigen is of molecular weight of 72 kD and the antigen is a colon carcinoma associated antigen and an ELISA for detection of the antigen in samples was performed

and the antibody was labeled with an enzyme. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have labeled the antibody and produce a chimeric antibody in view of Hollinshead et al and Neuberger et al because Neuberger et al teach labeling of antibodies for detection and treatment with cytotoxic agents and radiolabels and the antibodies are chimeric antibodies. Thus, it would have been obvious to one of ordinary skill in the art to produce a chimeric antibody which is a labeled antibody to the antigen of Hollinshead in view of Neuberger et al.

Although claims 30-33, 36-37 recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, and methods of detectably labeling antibodies and derivatives thereof also were well known and available to the ordinarily skilled artisan.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Hollinshead et al's antigen is described as being a colon carcinoma antigen which induces an immune response and is not present in normal tissue. Hollinshead et al is silent as to the method of purification of the antigen , however, it is the Examiner's position that Hollinshead et al have produced hybridomas which secrete antibodies that are directed to the same antigen that the claimed antibodies bind. One of ordinary skill in the art would reasonably conclude that Hollinshead's antibody also possesses the

same structural and functional properties as those of the antibodies claimed and, therefore, it appears that Hollinshead have produced hybridomas that secrete antibodies that are identical to the claimed antibody and bind the same antigen claimed. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody of Hollinshead, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The response filed 3/15/04 has been carefully considered but is deemed not to be persuasive. The response states that as indicated above, Hollinshead, fail to teach antibodies having the limitations set forth in the claims thus there can be no obvious rejection (see page 10-11 of response). In response to this argument, the Hollingshead reference was addressed above and thus the rejection is proper. In addition it would be obvious to use a secondary antibody for detection as taught in Neuberger.

27. Claims 1, 7-23, 30-33, 36-37, 42, 45, 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herlyn et al (PNAS 76:1138, 1979) or Price et al (IRCS Journal of Medical Science 13:366, 1985) and further in view of Neuberger et al (WO 86/01533, published 3/86).

The claims have been described supra. Claims 16-22 and 46 are included in the rejection and are interpreted to mean an antibody that binds to the Fc region of antibody in claims 1-6 and 42 which is interpreted to be a secondary antibody.

Herlyn et al and Price et al have been described supra. Both Herlyn et al and Price et al teach secondary antibodies which are anti-Ig antibodies (see page 1439 of Herlyn and page 366 of Price). Herlyn et al and Price et al do not teach chimeric antibody or an antibody labeled with a cytotoxin, radiolabel, a kit comprising an antibody and a second antibody and a substrate for the enzyme, or a method of diagnosing colon cancer with a chimeric antibody. These deficiencies are made up for in the teaching of Neuberger et al.

Neuberger et al teach chimeric antibodies and antibodies that can be labeled with toxins, radiolabels, dyes, cytotoxic agents (see page 7) and the antibody can be immobilized for affinity chromatography (see page 8).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have labeled the antibody and produce a chimeric antibody in view of Herlyn et al or Price et al in view of Neuberger et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have labeled the antibody and produce a chimeric antibody in view of Herlyn et al or Price et al et al and Neuberger et al because Herlyn et al or Price et al teach a colon carcinoma antigen and detection of the antigen. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have labeled the antibody and produce a chimeric

antibody in view of Herlyn et al or Price et al and Neuberger et al because Neuberger et al teach labeling of antibodies for detection and treatment with cytotoxic agents and radiolabels and the antibodies are chimeric antibodies. Thus, it would have been obvious to one of ordinary skill in the art to produce a chimeric antibody which is a labeled antibody to the antigen of Herlyn et al or Price et al in view of Neuberger et al.

Although claim s 30-33, 36-37 recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, and methods of detectably labeling antibodies and derivatives thereof also were well known and available to the ordinarily skilled artisan.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Price teach the antigen is a colon carcinoma antigen and is not in normal tissue and it would obviously induce an immune response because the antigen is foreign and Price is silent as to the purification characterization of the antigen.

Herlyn is silent as to the purification characterization of the antigen but teaches the antigen is from colon carcinoma cells and does not bind to normal cells and the antigen would obviously induce an immune response because it is a foreign antigen.

However, it is the Examiner's position that Herlyn or Price have produced hybridomas which secrete antibodies that are directed to the same antigen that the claimed antibodies bind. One of ordinary skill in the art would reasonably conclude that

Herlyn's or Price's antibody also possesses the same structural and functional properties as those of the antibodies claimed and, therefore, it appears that Herlyn or Price have produced hybridomas that secrete antibodies that are identical to the claimed antibody and bind the same antigen. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody of Herlyn or Price, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The response filed 3/15/04 has been carefully considered but is deemed not to be persuasive. The response states that as indicated above each of Herlyn, Hollinshead, and Price fail to teach antibodies having the limitations set forth in the claims thus there can be no obvious rejection (see page 10-11 of response). In response to this argument, the Herlyn and Price references were addressed above and thus the rejection is proper.

28. The specification and claims have been amended and as such a new oath/declaration is required. In accordance with 37 CFR 1.175(b)(1), a supplemental reissue oath/declaration under 37 CFR 1.175(b)(1) must be received before this reissue application can be allowed.

In addition, there are several problems with the oath/declaration as follows and applicant is requested to review the oath/declaration for other problems:

(1). It does not say they reviewed and understand the amendments (see 37 CFR 1.63(b)(1).

(2). Priority claim in oath/declaration is incomplete as series codes are missing (i.e. 08, 09, 10).

(3). The oath/declaration does not state "applicant believes the original patent to be wholly (or partly) inoperative (or invalid)" it states ("potentially inoperative". See 37 CFR 1.175(a)(1).

(4). The error discussed in the oath or declaration is still not fixed in the claims. The Oath/Declaration states that the deposits of hybridoma cell lines HB-12314 and HB-12315 referred to in the '657 patent were deposited erroneously at the ATCC (see page 2-4 of Oath/Declaration). Because this error has not been corrected as indicated above the Oath/Declaration ids defective.

Claims 1-50 are rejected as being based upon a defective reissue oath/declaration under 35 U.S.C. 251. See 37 CFR 1.175. The nature of the defect is set forth above.

Receipt of an appropriate supplemental oath/declaration under 37 CFR 1.175 and 1.63 will overcome this rejection under 35 U.S.C. 251. An example of acceptable language to be used in the supplemental oath/declaration is as follows:

> "Every error in the patent which was corrected in the present reissue application, and is not covered by a prior oath/declaration submitted in this application, arose without any deceptive intention on the part of the applicant."

29. Claims 1-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1, 30, 34, 38 and those claims depending on these claims are indefinite for reciting "membrane fractions" because it is unclear what the membrane fraction is. Is the antigen in the membrane fraction or not and what is the membrane fraction? In addition these claims are also indefinite for reciting "substantially free from non-immunogenic glycoprotein fraction". Does the phrase mean all glycoproteins were removed and if so how can claim 6 recite that the antigen is a glycoprotein?

b. Claims 16-21 and 46 are indefinite for reciting "A monoclonal antibody against the monoclonal antibody" because does the phrase mean an anti-idiotype antibody or an anti-IgG antibody or anti-Fc antibody? What does the antibody bind to?

c. Claims 1, 30, 34, 38 and those claims depending on these claims are indefinite for reciting "normal colon cancer free human tissue" because does the phrase mean tissue without cancer or tissue without colon cancer?

d. Claims 30-41 are indefinite for reciting "second antibody to said antigen or an active component thereof" in claims 30, 34, 38 because it is not clear what an active component of an antigen is. In addition, is the active component directed to the second antibody or to the antigen?

e. Claim 6 lacks antecedent basis for reciting "said colon carcinoma-associated antigen" in claim 2 because claim 2 recites a "colon carcinoma-associated epitope" not antigen.

f. Claims 4-5, 19-20, 23, 25, 27, 28, 34-37 are indefinite for reciting "antibody 31.1 (ATCC HB-12314)" in claims 4, 23, 25, 28, 34 because it is unclear if this antibody is the same as "PCA 31.1" as stated in the specification as ATCC "PTA-2497".

g. Claims 2, 22, 24, 29, 38, and those claims depending on these claims are indefinite for reciting antibody "33.28 (ATCC HB-12315)" because it is unclear if this antibody is the same as "PCA 33.28" as stated in the specification.

30. Claims 2-6, 17-29, 34-41 are rejected under 35 U.S.C. 251 as being based upon new matter added to the patent for which reissue is sought. The added material which is not supported by the prior patent is as follows:

Claims 4, 23, 25, 28, and 34 recite "antibody 31.1 (ATCC HB-12314) and the specification discloses "PCA 31.1" as stated in the specification as ATCC "PTA-2497" and as stated above it is not clear if these are the same antibodies. In addition claims 2, 22, 24, 29, and 38 recite antibody '33.28 (ATCC HB-12315)" and the specification teaches "PCA 33.28" and as stated above it is not clear if these two antibodies are the same. If the material is not the same then the amendment adds new matter to the specification.

31. Claims 2-6, 17-29, 34-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claims 4, 23, 25, 28, and 34 recite "antibody 31.1 (ATCC HB-12314) and the specification discloses "PCA 31.1" as stated in the specification as ATCC "PTA-2497" and as stated above it is not clear if these are the same antibodies. In addition claims 2, 22, 24, 29, and 38 recite antibody '33.28 (ATCC HB-12315)" and the specification teaches "PCA 33.28" and as stated above it is not clear if these two antibodies are the same. If the material is not the same then the amendment adds new matter to the specification. Applicants are required to provide specific support for the limitations in the specification as originally filed or remove it from the claims.

32. Claims 16-21, 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an anti-Fc or an anti-IgG antibody that binds to the a monoclonal antibody of claims 1-6 and 42, does not reasonably provide enablement for any anti-idiotypic antibody that binds the monoclonal antibody of claims 1-6 or claim 42. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to any anti-idiotypic antibody to the antibody of claims 1-6 and 42.

The specification does not disclose any working examples of an anti-idiotype antibody to an antibody of claims 1-6 and 42,

The claims encompass anti-idiotypic antibodies that bind to any antibody of claims 1-6 and 42 . Raychaudhuri S. U.S. Patent 5,270,202 acknowledges that the successful production of anti-idiotypic antibodies is an unpredictable endeavor (see column 3, lines 35-54). "In short, the discovery of therapeutically useful anti-idiotypic antibodies is as much art as science" (see column 3, lines 49-51). Chatterjee et al (U.S. Patent 6,235,280 B1) teach that not all anti-idiotype antibodies can be used in therapeutic regimens against tumors. First, only a fraction of antibodies raised against an Ab1 (anti-antigen antibody) are limited in their reactivity to the paratope of Ab1 (i.e., are non-reactive against features shared with other potential antibodies in the host). Second, anti-idiotype antibodies are not necessarily immunogenic. Third, only a fraction of the immunogenic anti-idiotypes elicit an antigen-specific immune response. Further,

anti-idiotype therapy with respect to tumor origin and antigens expressed should be evaluated on a case-by-case basis since different cancers have widely varying molecular and clinical characteristics (see column 2, lines 39-53). Thus, without producing such anti-ids the prior art concludes that it would be unpredictable to produce such for therapy as speculated in the specification.

Applicants have provided insufficient evidence or nexus that would lead the skilled artisan to predict the ability to use just any anti-idiotypic antibody to just any antibody of claims 1-6 and 42. One of skill in the art would neither expect nor predict the appropriate functioning of the anti-idiotypic antibodies as broadly as is claimed.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to any anti-idiotypic antibody to any antibody that binds the antibodies of claims 1-6 and 42.

Conclusion

33. No claim is allowed.

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571)

272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (571) 272-0871.

35. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832